REMARKS

With entry of the current amendment the application will contain claims 4-6 and 13-18. Amongst these claims, only claims 4 and 6 are independent. All other claims are either directly or indirectly dependent upon claim 1.

The courtesies extended to Applicant's representative, David R. Murphy, during a telephone interview on or about January 29, 2003 are acknowledged with appreciation. The following remarks incorporate the substance of the items discussed during that telephone interview.

Election/Restriction

The requirement for restriction is traversed for the reasons of record.

Abstract

A new Abstract has been provided herewith as Exhibit B rendering moot the Examiner's objections beginning on page 3 of the last Office Action.

Claim 6 is allowable

The attention of the Examiner is respectfully invited to the sentence on the first line of page 4 of the last Office Action

wherein it is indicated that the elected compound was not found in the search. The elected compound is the compound of claim 6. On the other hand page 1, paragraph 4a of the last Office Action indicates that claims 2-18 are withdrawn from consideration. This would, of course, include claim 6. When this was discussed with the Examiner, the Examiner indicated that claim 6 should have been indicated as being allowable. The Examiner is respectfully requested to clearly indicate the allowability of 6 in his response to this reply.

Rejections under 35 U.S.C. 102

In the last Office Action the only claim rejected under 35 U.S.C. 102 was claim 1. No other claim was rejected. Since claim 1 has been cancelled this ground of rejection is moot. It is respectfully submitted that all pending claims define subject matter which is novel over all references of record.

Mikhailov, A.S. et al. describes the preparation of dimmers of 2-thio-6-methyl-4-pyrimidinyl and bridged amino-pyrimidine derivatives having a di-thiol as bridging group. No biological data are presented. The cyclic amino-quinazoline derivatives of the present invention are not suggested.

Rejections under 35 U.S.C. 112

In the last Office Action only claim 1 was rejected under 35 U.S.C. 112. Since this claim has been cancelled, this ground of rejection is moot. Even though this ground of rejection is moot, a concerted effort has been made to ensure that pending independent claim 4 is free of the grounds of rejection previously levied against claim 1.

The language objected to in paragraph (i) on page 5 of the Office Action does not appear in claim 4.

It is believed that the definitions of A and B in independent claim 4 are free of the objections made against claim 1 in paragraph (ii) on page 5 of the last Office Action.

In paragraph (iii) on page 5 of the last Office Action the Examiner objected to the word "carbocyclic". That term does not now appear in independent claim 4 such that claim 4 is free of this ground of rejection.

In paragraph (iv) on page 5 of the last Office Action the Examiner objected to the word "heterocyclic". That term does not now appear in independent claim 4 such that claim 4 is free of this ground of rejection.

Neither the term "hetero-alkyl" nor the term "amido" is present in independent claim 4. Thus, claim 4 is free of the

objections made against claim 1 on page 6 in paragraph (v) and (vi) of the last Office Action.

A Final Rejection Would Be Premature

The undersigned takes note of the following statement in the last Office Action:

> As in the prevailing practice, **a second action on the rejected claims would be made final.**
>
> As an example, in the case of an application with a Markush-type claim drawn to the compound C - R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the Examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the non-elected species would be held withdrawn from further consideration.
>
> (Office Action mailed 02/21/2003; page 4, line 13; emphasis in original).

Strenuous objection is made of the absence of an Office Action on the merits as to claim 4 originally filed. In response to the requirement for restriction, the species of allowable claim 6 was elected.

Both claims 1 and 4 were generic to the subject matter of allowable claim 6. Even assuming arguendo that claim 1 is properly

rejectable, the Examiner should not have stopped his search and should have extended his search at least to the subject matter of generic claim 4.

While it is true that claim 4 has been amended it has only been slightly amended in two ways. The first way is that it is now independent. The second way is that the term "amido" has been voluntarily amended in order to advance prosecution such that claim 4 would not be objectionable for reasons that the Examiner applied against claim 1. These two minor amendments to claim 4 do not require additional search by the Examiner. Claim 4 should have been searched in response to the first Office Action.

In summary it is respectfully submitted that all pending claims are allowable and that the Examiner would be justified in passing the case to issue. If, however, the Examiner deems it appropriate to issue another Office Action, that Office Action should be "Non-Final".

Conclusion

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact David R. Murphy (Reg. No. 22,751) at the telephone number of the undersigned below, to conduct an interview

in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of $110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
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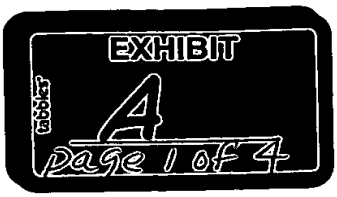
GMM/DRM/jmb
2815-0187P

Attachment(s): Exhibit A (4 pages) being all pending claims submitted as provided in the waiver to 37 C.F.R. 1.121
Exhibit B Abstract

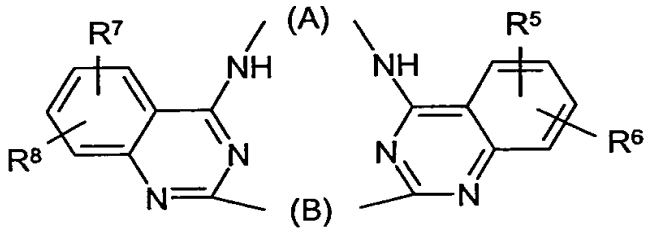
CLAIMS

CLAIMS 1-3 HAVE BEEN DELETED



(currently amended)

4. ~~The bridged amino-pyrimidine derivative of claim 1, which is a 2,4-bridged bis-4-amino-quinazoline derivative~~A compound ~~represented by the~~of general Formula II,



(II)

wherein

A and B, independently of each another, represent
a linear or branched alkylene chain having of from 1 to 15 carbon atoms, which alkylene group may be interrupted by one or more oxygen or sulphur atoms, or by one or more groups of the formula -NR'''-, or =NR''', wherein R''' represents hydrogen or alkyl; or
a di-radical of the formula $-(CH_2)_a-D-(CH_2)_b-$, wherein a and b, which may be identical or different, represent the number 0, 1, 2, 3, 4 or 5, and D represents a cycloalkyl group, or an aryl group of from 6 to 12 carbon atoms, which aryl group may in particular be a phenyl group or a biphenyl group; and

R^5, R^6, R^7 and R^8, independently of each another, represent
hydrogen, halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or ~~amide~~H-CO-NH-, alkyl-CO-NH-, H-CO-N(alkyl)- or alkyl-CO-N(alkyl)-, or a group of the formula -R', -OR', -SR', -R'OR'', -R'SR'', -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', or -C(S)SR'; or

4

a phenyl or a phenoxy group, which phenyl or phenoxy groups may optionally be substituted on or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or ~~amido~~H-CO-NH-, alkyl-CO-NH-, H-CO-N(alkyl)- or alkyl-CO-N(alkyl)-, or a group of the formula -R', -OR', -SR', -R'OR", -R'SR", -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', or -C(S)SR';

wherein R' and R", independently of each another, represent hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or alkoxyalkyl, or a group of the formula NR'"R"", wherein R'" and R"", independently of each another, represent hydrogen or alkyl.

5. (currently amended) The ~~bridged amino-quinazoline derivative~~compound of claim 4, wherein A and B, independently of each another, represent

decamethylene; octamethylene; hexamethylene; pentamethylene; tetramethylene; trimethylene; dimethylene; N,N'-dimethyl-diamino-methylene; N,N'-dimethyl-diamino-dimethylene; N,N'-dimethyl-diamino-trimethylene; (cis and/or trans)-1,5-cyclooctylene; (cis and/or trans)-1,3-dimethylcyclohexane-α,α'-diyl; para-xylene-α,α'-diyl; meta-xylene-α,α'-diyl; 1,3-phenylene; biphenyl-3,3'-diyl; 4,4'-dimethyl-bibenzyl-α,α'-diyl; 4,4'-dimethyl-diphenylmethane-α,α'-diyl; 4,4'-dimethyl-cis/trans-stilbene-α,α'-diyl; 2,6-bis(4'-methyl-phenyl)pyridine-α,α'-diyl; 3,3'-dimethyl-biphenyl-α,α'-diyl; or 2,7-dimethyl-9H-fluorene-α,α'-diyl.

6. (currently amended) The ~~bridged amino-quinazoline derivative~~compound of ~~claim 4, being 20,23-dimethyl-2,10,18,20,23,25,32,33-octaazahexacyclo-[22.7.1.1^{4,8}.1^{11,19}.0^{12,17}.0^{26,31}]-tetratriaconta-1(32),11,13,15,17,19(33),24,26,28,30-decaene~~the formula

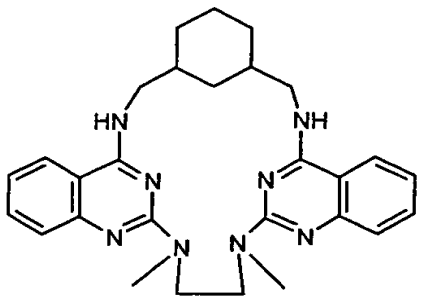


EXHIBIT A page 2 of 4

CLAIMS 7 - 12 HAVE BEEN DELETED

13. (original) A chemical compound according to claim 1, for use as a medicament.

14. (original) The use of a chemical compound according to claim 1 for the manufacture of a medicament for the treatment, prevention or alleviation of a disease or a disorder or a condition of a mammal, including a human, which disease, disorder or condition is associated with the activity of potassium channels.

15. (original) The use according to claim 14, wherein the disease or disorder is asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhoea, ischaemia, cerebral ischaemia, ischaemic heart disease, angina pectoris, coronary heart disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labour, baldness, cancer, and immune suppression.

16. (original) A pharmaceutical composition comprising a therapeutically-effective amount of a chemical compound according to claim 1, or a pharmaceutically-acceptable addition salt thereof, together with at least one pharmaceutically-acceptable carrier or diluent.

17. (original) A method of treatment, prevention or alleviation of a disease or a disorder or a condition of a living animal body, including a human, which disease, disorder or condition is responsive to blockade of the potassium channel, and which method comprises comprising administering to such a living animal body, including a human, in need thereof a therapeutically-effective amount of a compound of claim 1.

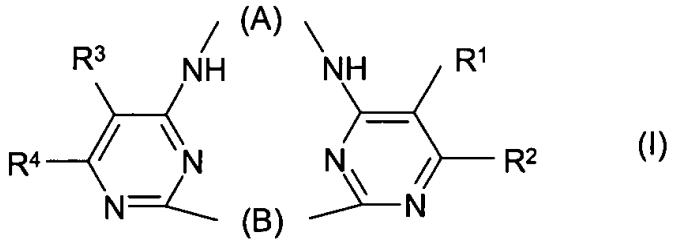
(original) ~~6~~

18. /1 The method according to claim 17, wherein the disease or disorder or condition is asthma, cystic fibrosis, chronic obstructive pulmonary disease and rhinorrhea, convulsions, vascular spasms, coronary artery spasms, renal disorders, polycystic kidney disease, bladder spasms, urinary incontinence, bladder outflow obstruction, irritable bowel syndrome, gastrointestinal dysfunction, secretory diarrhoea, ischaemia, cerebral ischaemia, ischaemic heart disease, angina pectoris, coronary heart disease, traumatic brain injury, psychosis, anxiety, depression, dementia, memory and attention deficits, Alzheimer's disease, dysmenorrhea, narcolepsy, Reynaud's disease, intermittent claudication, Sjorgren's syndrome, migraine, arrhythmia, hypertension, absence seizures, myotonic muscle dystrophia, xerostomi, diabetes type II, hyperinsulinemia, premature labour, baldness, cancer, and immune suppression.

C 1

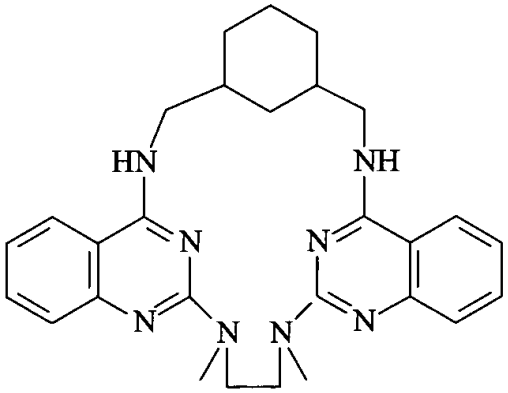
ABSTRACT

Compounds of Formula I:



(I)

wherein A and B are linking groups; R^1, R^2, R^3 and R^4 are defined moieties. An exemplary compound is:



These compounds function as potassium channel blocking agents, and can be used in a wide variety of pharmaceutical compositions for the treatment of a wide variety of diseases.

EXHIBIT
tabbies
B